REMARKS:

Claims 1-3, 5, 13-15, 17, 19-23, 25 and 27-31 were rejected under 35 USC 103(a) as unpatentable over Ito as applied to claims 1-3, 5 and 30-31 and further in view of Kahn.

The previous office action states that Kahn 'teaches a recombinant vesicular stomatitis virus (VSV) expressing foreign glycoproteins that elicit specific protective immunity (Abstract). Kahn teaches the VSV glycoprotein (G) gene was deleted from the full-length cDNA VSV genomic plasmids containing the RSV G gene such that the RSV G genes replaced VSV G in viral genome... The RSV G (attachment) is the first and major antigenic glycoprotein...'

The office action further states that 'it would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to prepare the immunogenic composition in an animal and use the composition to elicit an immune response. The person of ordinary skill in the art would have been motivated to make use of a VSVΔG to elicit an immune response because Ito teaches it is effective with Ebola (VHF), and reasonably would have expected success because of the teachings of Kahn'.

n the response to arguments section, the instant office action states that 'Kahn teaches a recombinant VS expressing foreign proteins. Kahn teaches the RSV G replaced the VSV G (glycoprotein) in the viral genome and particle.' The office action further states that 'Ito teaches a recombinant VSV wherein the Ebola virus glycoprotein was incorporated into recombinant VS particles. The combination of references teaches the instant claimed invention'.

Applicants respectfully note that at page 11082, column 1, 1st paragraph, Kahn states that 'the infectivity of these viruses is therefore based on the presence of VSV G which is supplied in trans by the BHK G cell line.' Thus, Kahn

does not teach a particle in which only the VHF glycoprotein is expressed as in Kahn, both the RSV and VSV G proteins are present.

Furthermore, applicants note that neither Kahn nor Ito teach a particle which is infectious, that is, capable of multiple rounds of infection. In both cases, the particles are capable of cell entry by virtue of glycoproteins supplied in trans.

The combination of Ito and Kahn thus would suggest substitution of Ebola GP for RSV with VSV G being supplied in trans. As discussed above, that is not applicants' invention, as the Ebola (VHF) GP would not be the only glycoprotein present on the particle.

Furthermore, the prior art teaches against the combination of an infectious particle expressing a viral hemorrhagic fever glycoprotein. Specifically, attached is the abstract for Yang et al., 2000, Nat Med 6(8): 886-889 which states that the main viral determinate of Ebola virus pathogenicity is the glycoprotein and the glycoprotein likely contributes to hemorrhage during infection. Accordingly, one of skill in the art would conclude that such a particle would be capable of endothelial cell disruption and/or cytotoxicity in view of the Yang et al reference.

Surprisingly, as discussed at least at page 6, lines 25-27 of the application as filed, applicants have developed an infectious system that simulates infection with the foreign virus and yet does not cause disease or the symptoms associated with the foreign virus.

As discussed above, applicants again note that the prior art does not teach an infectious virus particle wherein a VHF glycoprotein is the only glycoprotein present on the particle surface. Ito teaches a particle wherein the VHF is supplied in trans and Khan teaches a particle in which both RSV and VSV proteins are present. Furthermore, as discussed above, there were concerns regarding the properties of an

infectious particle expressing a VHF glycoprotein as discussed above. However, applicants discovered that that was not the case.

In view of the foregoing, further and more favorable consideration is respectfully requested.

Respectfully submitted
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1: Nat Med. 2000 Aug;6(8):886-9.

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Identification of the Ebola virus glycoprotein as the main viral determinant of vascular cell cytotoxicity and injury.

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Here we defined the main viral determinant of Ebola virus pathogenicity; synthesis of the virion glycoprotein (GP) of Ebola virus Zaire induced cytotoxic effects in human endothelial cells in vitro and in vivo. This effect mapped to a serine-threonine-rich, mucin-like domain of this type I transmembrane glycoprotein, one of seven gene products of the virus. Gene transfer of GP into explanted human or porcine blood vessels caused massive endothelial cell loss within 48 hours that led to a substantial increase in vascular permeability. Deletion of the mucin-like region of GP abolished these effects without affecting protein expression or function. GP derived from the Reston strain of virus, which causes disease in nonhuman primates but not in man, did not disrupt the vasculature of human blood vessels. In contrast, the Zaire GP induced endothelial cell disruption and cytotoxicity in both nonhuman primate and human blood vessels, and the mucin domain was required for this effect. These findings indicate that GP, through its mucin domain, is the viral determinant of Ebola pathogenicity and likely contributes to hemorrhage during infection.

PMID: 10932225 [PubMed - indexed for MEDLINE]